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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/050,704	01/18/2002	Steven M. Ruben	PZ039P1C1	8649

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HUMAN GENOME SCIENCES INC
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EXAMINER
JIANG, DONG

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 07/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/050,704	RUBEN ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11,12,19,20 and 24-56* is/are pending in the application.

4a) Of the above claim(s) *19, 20 and 24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11,12 and 25-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *11,12,19,20 and 24-56* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED OFFICE ACTION

Applicant's election with traverse of Group II invention, represented by the original claims 11, 12 and 16, in Paper No. 5, filed on 08 May 2003 is acknowledged. The traversal is on the ground(s) that searching all of groups I-X do not constitute a serious burden, and that although groups I-X are separately classified, a search of the claims of any of the groups would also provide useful information for the claims of the other groups. This is not found persuasive because according to MPEP, a serious burden may be established by (A) separate classification thereof; (B) a separate status in the art when they are classifiable together; or (C) a different field of search. In the instant case, Groups I-X are patentably distinct inventions as shown by their separate classification, indicating each distinct subject has attained recognition in the art as a separate subject for inventive effort, and also a separate field of search. As stated in the MPEP 803, "a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP 802.02.". Further, a search is directed not only to art, which would be anticipatory, but also to art that would render the invention obvious. Therefore, it is insufficient to search for one group and try to apply the result for other groups even though a search of the claims of any of the groups may provide useful information for the claims of the other groups. As such, all groups require divergent searches, and to search all groups of inventions would constitute serious burden. Further, applicants have canceled the non-elected claims 1-10, 13-18 and 21-23, indicating that the traversal of the restriction requirement among the groups consisting of these claims is irrelevant.

With respect to applicants request for rejoinder of groups VI, VII and X, as they are drawn to the product and the processes for using the product, as no claims have been indicated to be allowable, this request will be held in abeyance until such time.

The requirement is still deemed proper and is therefore made FINAL.

Applicant's amendment in paper No. 5, filed on 08 May 2003 is acknowledged and entered. Following the amendment, claims 1-10, 13-18 and 21-23 are canceled, and the new claims 25-56 are added.

Currently, claims 11, 12, 19, 20 and 24-56 are pending, and claims 11, 12 and 25-56 are under consideration. Claims 19, 20 and 24 are withdrawn from further consideration as being drawn to a non-elected invention.

Formal Matters:

Claim 11 is objected to for encompassing a non-elected subject matter, SEQ ID NO:X and Y, and ATCC Deposit No.:Z. The applicant is required to amend the claims to read only upon the elected invention.

In the interest of compact prosecution, the claims will be examined as though drawn to the elected invention.

Objections and Rejections under 35 U.S.C. §101 and §112:

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 11, 12 and 25-56 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a credible, substantial, and specific, or a well-established utility.

The elected invention is an isolated polypeptide with SEQ ID NO:125, variants and fragments thereof, and composition thereof. Said polypeptide is encoded by a cDNA clone designated HOFND85.

The specification discloses a polypeptide of HOFND85 having an amino acid sequence of SEQ ID NO:125, which is encoded by the polynucleotide of SEQ ID NO:39. The specification asserts that the polypeptide shares sequence homology with the superfamily of protocadherin proteins relating to cadherin, that when tested against both Jurkat T cells and U937 myeloid cell lines, the supernatants removed from cells containing this gene activated the GAS assay, indicating the involvement of the protein in the proliferation and differentiation of cells (page 82, lines 17-22, and lines 27-29), that this gene is expressed primarily in ovarian tumor, indicating a role in the regulation of cellular division, and usefulness for differential identification of the tissues or cells, the detection, diagnosis, treatment, and/or prevention of

. developmental diseases and disorders including cancer and other proliferative conditions (page 82, line 30, and page 83, lines 2-4, and 16-20), and that the protein may show utility as a tumor marker and/or immunotherapy targets (page 83, lines 12-14).

The asserted utilities discussed above are not considered to be substantial for the following reasons.

With respect to the involvement of the protein in the proliferation and differentiation of cells, it is not specific nor substantial because it is unclear whether the activity is due to the direct effect of the HOFND85 protein as the supernatants may contain many other molecules or factors, which may contribute to the outcome of the assays. Therefore, the results form such assays are not specific and substantial. Further, even if the HOFND85 protein were responsible for the cell proliferation and differentiation events, it is not specific as many proteins and growth factors can stimulate proliferation and differentiation of cells.

With respect to the use of the polypeptide as a tumor marker, the Examiner is not able to locate the supporting evidence in the specification, i.e., Table 2 illustrating the tissue distribution of a number of proteins claimed in the present application does not contain the information for the HOFND85. Further, the specification indicates that this protein is also expressed in normal ovarian tissue, implicating a role in normal ovarian function, and potential usefulness in the treatment of female infertility, or as a female contraceptive (page 84, lines 22-25). As the HOFND85 is expressed in both normal and ovarian tumor tissues, the Examiner is not able to conclude that the HOFND85 is suitable as a tumor marker in the absence of any supporting evidence and statistical analysis as to the difference in expression between the normal and ovarian tumor tissues. Undue experimentation is required to determine such use, and therefore, the asserted utility as a tumor marker is not substantial. Upon further research, a specific, and substantial utility might be found for the claimed polypeptide. This further characterization, however, is part of the act of invention, and until it has been undertaken, the claimed invention is incomplete. Thus, there was no immediately apparent or "real world" utility and the claimed invention is incomplete as of the filing date.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11, 12 and 25-56 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

In addition, even if there were utility and enablement of the polypeptide having SEQ ID NO:125, enablement would not be commensurate in scope with the claims, which encompass various variants (claims 11, 12, and 37-46, for example), and fragments (11, 12, and 47-56, for example) of SEQ ID NO:125 or of the polypeptide encoded by the cDNA PTA-1544. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 11, 12, and 37-56 are directed to variants at least 95% or 90% sequence identical to SEQ ID NO:125, or to the polypeptide encoded by cDNA PTA-1544, and fragments of at least 30 contiguous amino acids thereof, which read on any or all variants meeting the sequence limitation, or any randomly selected fragment, with or without functional activity. The specification does not teach how to use any of the variants or fragments of HOFND85 polypeptide. Since a biological function of HOFND85 polypeptide is not disclosed in the specification, and since one skilled in the art could not determine with a reasonable expectation of success what a specific or substantial biological function of HOFND85 polypeptide would be, the skilled artisan would not be able to make functional variants or fragments of HOFND85 polypeptide, and test them for a biological activity, because one is not disclosed. Furthermore, the specification provides no guidance as to how the skilled artisan could use an inactive variant or fragment of HOFND85 polypeptide, as no functional limitation associated with these variants or fragments in the claims. Therefore, it would require undue experimentation to practice this invention as claimed, because the skilled artisan would have no reasonable expectation of being

able to use the variants or fragments of HOFND85 polypeptide for any purpose stated in the specification.

Claims 11, 12, and 37-56 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 11, 12, and 37-56 encompass % variants, a secreted form, a variant, an allelic variant, a species homologue, or fragments of said polypeptide. The claims do not require that the polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides that is defined only by sequence identity. The specification merely discloses *one* amino acid sequence of the HOFND85 with SEQ ID NO:125. No variants or fragments thereof meeting the limitation of the claim were ever identified or particularly described.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

In the instant application, applicants have a single polypeptide with a specific function that have not been correlated to any particular structural regions. Therefore, only isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO:125, but not the full breadth of the claims (variants and fragments) meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 11, 31-34, 42-46, and 52-56 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 11, 31-34, 42, 44, and 52-54 recite a deposit of a cDNA clone encoding said protein contained in ATCC Deposit No. PTA-1544. However, the specification fails to provide the deposit statement indicating the deposit material will be readily available to the public without restriction upon issuance of the patent. Such statement would satisfy the enablement requirement of 35 U.S.C. 112.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating

(a) that the deposit has been made under the terms of the Budapest Treaty; **and**

(b) that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent,

would satisfy the deposit requirements. See 37 C.F.R. 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then the requirements may be satisfied by an affidavit or declaration by Applicants or someone associated

with the patent owner who is in a position to make such assurances, or by a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and establishing that the following criteria have been met:

(a) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 C.F.R. 1.807 is provided; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination, or loss of capability to function described in the manner in the specification.

In either case, the identifying information set forth in 37 C.F.R. 1.809(d) should be added to the specification if it is not already present. For deposits made with the ATCC, note that effective 23 March 1988 the depository's address is:

American Type Culture Collection
10801 University Boulevard
Manassas, VA 20110-2209

See 37 C.F.R. 1.803-1.809 for additional explanation of these requirements.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11, 12, 29, 35, 40, 45, 50 and 55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 is indefinite for the following reasons:

1) The claim recites limitations as "X, Y, and Z", and it is not clear what sequences are indicated. The metes and bounds of the claim, therefore, cannot be determined.

2) It is not clear what is a polypeptide *domain* in part c) of the claim, and the specification does not define such. The metes and bounds of the claim, therefore, cannot be determined.

3) It is not clear what is "a secreted form" in part (e), or "a variant" in part g). "A secreted form" of a protein may vary depending upon cell types from which the protein is produced. The metes and bounds of the claim, therefore, cannot be unambiguously determined.

Claim 12 is indefinite because it is unclear how many sequential amino acid deletions can be made from either end. The metes and bounds of the claim, therefore, cannot be determined.

Claims 29, 35, 40, 45, 50 and 55 are indefinite for the recitation of "an *acceptable* carrier" because it is unclear what it is acceptable for.

The remaining claims are rejected for depending from an indefinite claim.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11, 47, 50-52, 55 and 56 are rejected under 35 U.S.C. 102(b) as being anticipated by Suzuki, WO 96/00289 (04 January 1996).

Suzuki discloses a polypeptide sequence of human protocadherin pc3 having SEQ ID NO:110, which comprises residues 588-627 of SEQ ID NO:125 of the present invention with 100% sequence identity (see computer printout of the search results). Thus, the cited sequence anticipates claims 11, 47 and 52 as being a polypeptide at least 95% identical to a polypeptide fragment of SEQ ID NO:125 (claim 1, part (a), for example), or to a epitope of SEQ ID NO:125 (claim 1, part (d), for example), or a protein consisting of at least 30 contiguous amino acid residues of SEQ ID NO:125 (claim 47, for example) or of the complete polypeptide encoded by the HOFND85 cDNA (claim 52, for example). Additionally, Suzuki teaches a method for

producing said polypeptide by expressing the polypeptide by a cell, and isolated the polypeptide from the medium (claim 14). Thus, the reference also anticipates claims 51 and 56. With respect to claims 50 and 55, although Suzuki does not explicitly teach a composition comprising said protein and *an acceptable carrier*, however, it is well known in the art that a purified protein agent is usually used in combination with other agent(s), such as dissolving solutions, rather than used as its crystal form alone. Dissolving solutions, such as water, buffers, or media, meet the limitation of being "an acceptable carrier". Thus, the reference anticipates the claims.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 49 and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Suzuki, WO 96/00289, as applied to claims 11, 47, 50-52, 55 and 56 above, and further in view of Capon et al., US5,116,964.

The teachings of Suzuki are reviewed above. The primary reference does not teach a fusion protein comprising said polypeptide and a heterologous sequence.

Capon discloses a novel polypeptide comprising an immunoglobulin Fc region, and a target protein sequence (column 5, lines 13-20). The cited reference indicates that fusion of a target protein to heterologous peptide such as a stable plasma protein such as an immunoglobulin constant domain extends the in vivo plasma half-life, and facilitate purification of the protein (column 4, lines 38-43, and column 5, lines 13-20).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to use the amino acid sequence of Suzuki to make a fusion polypeptide comprising said peptide and an Ig constant region sequence as taught by Capon. One of ordinary skill in the art would have been motivated to make such a fusion polypeptide for the advantages taught by Capon, and reasonably would have expected success in view of Capon's disclosure, in

which various genes had already been expressed successfully in their systems at the time the invention was made.

Conclusion:

No claim is allowed.

Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

Dong Jiang, Ph.D.
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AU1646
6/25/03